REMARKS

Reconsideration of the present application in view of the present amendments and the following remarks is respectfully requested. Claims 42, 46-48, 51, and 57 are pending and currently under consideration. Applicants respectfully request clarification regarding the disposition of the claims. The Office Action Summary and Item 9 of the Action indicate that claims 47, 48, 51, and 57 are allowable. However, these claims stand provisionally rejected under the judicially created doctrine of double patenting and stand rejected under 35 U.S.C. § 102(e). In addition, the Action Summary indicates that claims 42 and 46 are withdrawn from consideration; however, Applicants cannot find any reference to withdrawal of these claims in the Detailed Action or in any prior communication from the PTO. Furthermore, the PTO has examined these claims in the Detailed Action. In this Response, Applicants have addressed the rejections of all claims in the Detailed Action even though the status of the claims appears inconsistent with the Action Summary. Applicants have amended claims 42, 47, and 51 and added new claims 113-117 to particularly point out and distinctly claim certain embodiments of Applicants' invention. Support for the amended and new claims may be found in the specification, for example, at page 18, lines 1-6; page 19, lines 19-27; page 20, lines 9-10; and the Sequence Listing. No new matter has been added.

DOUBLE PATENTING

Claims 42, 46-48, 51, and 57 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 42 and 46-57 of co-pending U.S. Patent Application No. 09/810,644, published as US 2002/0012992 (Anderson et al.), and as allegedly unpatentable over claims 42, and 46-48, 51, and 57 of co-pending U.S. Patent Application No. 09/185,904, published as US 2002/0177185 (Anderson et al.). The Action asserts that the pending claims are not patentably distinct from the claims co-pending in Application No. 09/810,644 and in Application No. 09/185,904, and that the ANT3 polypeptide and ANT3 fusion proteins claimed in the present application overlap the subject matter recited in the claims of the two co-pending applications.

The PTO further asserts that the ANT3 polypeptide claimed in the co-pending applications would be identical to the ANT3 polypeptide product-by-process recited in the claims.

Applicants respectfully traverse this rejection and submit that the present claims satisfy all requirements for patentability. Nevertheless, and solely in the interests of expediting prosecution, Applicants reserve the right to submit a terminal disclaimer at such time in the future as all other issues have been removed and the claims are otherwise in condition for allowance.

REJECTION UNDER U.S.C. § 102(e)

The PTO has rejected claims 42, 46-48, 51, and 57 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent Publication No. 2002/0177185 (Anderson et al., '185). In particular, the Examiner asserts that the ANT3 polypeptide described in Anderson et al. ('185) would be identical to the ANT3 polypeptide product-by-process recited in the present claims and would inherently possess the characteristics of the claimed ANT3 polypeptide.

Applicants respectfully traverse this rejection and submit that the claimed isolated recombinant ANT polypeptide comprising the amino acid sequence of a human ANT3 polypeptide as recited meets the requirement for novelty under 35 U.S.C. § 102(e). Anderson et al. (U.S. Pub. No. 2002/0177185, '185) is the parent application to which the present continuation-in-part application claims priority. Because Anderson et al. ('185) fully supports the subject matter of the instant claims, the '185 application was not filed "before" the invention of the subject matter that is presently claimed in the instant application. Hence, the claimed invention cannot be said to have been "described in an application for patent, published under section 122(b), by another filed in the United States *before* the invention by the applicant for patent". Applicants therefore believe that Anderson et al. ('185) is not properly cited under 35 U.S.C. §102(e) in the instant application. Nevertheless, if the Examiner still believes that §102(e) applies with regard to whether Anderson et al. ('185) represents an application "by another" (see M.P.E.P. §2136.04), Applicants respectfully submit that at the time of filing, the correct inventors were named in the present continuation-in-part application, but that as a result of the subsequent cancellation of several claims in the course of prosecuting the present

application, fewer than all of the currently named inventors are actual inventors of the presently claimed invention. Accordingly, Applicants respectfully submit that even in view of M.P.E.P. §2136.04, Anderson et al. will be removed as prior art upon Applicants' submission of an amendment under 37 C.F.R. § 1.48(b), requesting correction of inventorship to remove names of any persons who are not inventors of the invention presently being claimed. The amendment to correct inventorship will be forwarded to the PTO in due course to expedite prosecution of this matter, and until such time Applicants respectfully request that this issue be held in abeyance.

REJECTIONS UNDER 35 U.S.C. § 103(a)

The PTO rejects claims 42 and 46 under 35 U.S.C. § 103(a) as obvious over Cozens et al. (*J. Mol. Biol.* 206:261-80 (1989)) in view of Adrian et al. (*Mol. Cell Biol.* 6:626-34 (1986)). In particular, the PTO asserts that it would have been obvious for a person having ordinary skill in the art to express recombinantly the gene of Cozens et al. to obtain an isolated and purified ANT3 protein by a method such as the method taught by Adrian et al.

Applicants respectfully traverse this ground of rejection and submit that Cozens et al. and Adrian et al., alone or in combination, fail to teach or suggest the claimed invention. The present invention is directed, in pertinent part, to an isolated recombinant ANT polypeptide comprising the amino acid sequence of a human ANT3 polypeptide set forth in SEQ ID NO:33, wherein the ANT3 polypeptide localizes to a mitochondrial membrane and is capable of binding an ANT ligand. The isolated recombinant ANT polypeptide is produced by culturing a host cell comprising a recombinant expression construct that comprises at least one regulated promoter operably linked to a nucleic acid encoding the ANT polypeptide.

As an initial matter, Applicants wish to note that the instant rejections of claims 42 and 46 under 35 U.S.C. §103(a) appear in essence to be reiterations of rejections asserted by the PTO in an earlier Office Action dated December 2, 2002, to which rejections Applicants have previously responded. However, it is not clear that the PTO has considered all of Applicant's submissions of record. More specifically, the currently outstanding Office Action dated February 20, 2004, acknowledges the amendments to the claims in Applicant's preliminary amendment filed November 3, 2003, but the current Action is otherwise silent with respect to the

Remarks that were submitted along with the amendment on November 3, 2003, and the PTO further fails to acknowledge the Declaration of Christen M. Anderson under 37 C.F.R. §1.132 that was also submitted to the PTO on November 3, 2003. Applicants respectfully request that in addition to considering the Remarks submitted herewith, the PTO please reconsider the Remarks and the §1.132 Declaration that were previously submitted on November 3, 2003.

Applicants respectfully submit that the PTO has not established a *prima facie* case of obviousness. *See In re Mayne*, 104 F.3d 1339, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (PTO has the burden of showing a *prima facie* case of obviousness.). The PTO must show (1) that the references teach or suggest all claim limitations; (2) that the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior art to produce the claimed invention; and (3) that the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, a teaching, motivation, or suggestion to combine the references must exist. (*See In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

As discussed herein and for reasons already made of record, a *prima facie* case of obviousness has not been established because Cozens et al. and Adrian et al., each alone or in combination, fail to teach or suggest each and every limitation of the claims. Each document fails to teach or suggest an isolated recombinant human ANT3 polypeptide that comprises the amino acid sequence set forth in SEQ ID NO:33 or an isolated fusion protein that comprises a human ANT amino acid sequence at least 95% identical to human ANT3. As conceded in the Action, Cozens et al. fail to teach or suggest recombinant expression of ANT polypeptides and fail to teach or suggest the isolation of a recombinant ANT polypeptide. Cozens et al. only describe screening genomic libraries, determining the nucleic acid sequence of a gene that encodes a human ANT polypeptide, and then merely deducing its amino acid sequence. Adrian et al. also fail to teach or suggest recombinant expression of a full-length human ANT polypeptide or a human ANT fusion protein, wherein the ANT polypeptide has at least 95% identity to human ANT3 (SEQ ID NO:33). Adrian et al. merely describe expression of truncated

yeast ANT for determining if the ANT polypeptide is delivered to the mitochondria. Adrian et al. also fail to teach or suggest a recombinant expression system whereby the yeast ANT polypeptide, or any other ANT polypeptide, is expressed in a manner that permits isolation of the yeast ANT polypeptide from the yeast cells.

Moreover, neither document teaches or suggests the desirability of recombinantly expressing a human ANT polypeptide in a yeast cell or in any other host cell. Cozens et al. fail to teach or suggest or otherwise indicate the desirability of recombinantly expressing any ANT polypeptide. Similarly, Adrian et al. fail to teach or suggest the desirability of recombinantly expressing full-length yeast ANT polypeptide in yeast, much less teaching or suggesting the expression of a full-length ANT polypeptide from any other species. Both documents further fail to teach or suggest an isolated human ANT polypeptide that is cultured from a host cell that comprises a recombinant expression construct containing at least one regulated promoter that is operably linked to a nucleic acid encoding the human ANT polypeptide. Therefore, contrary to the assertion in the Action, neither Cozens et al. nor Adrian et al. provide a method by which to express members of the ANT family of proteins.

At best, the PTO's assertion of nonobviousness relies on the illegitimate test that an ordinarily skilled artisan might find it "obvious to try" to obtain the claimed recombinant human ANT polypeptide or fusion protein using the disclosure of any of the cited documents. *See In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) ("...[W]hether a particular combination might be "obvious to try" is not a legitimate test of patentability."). However, the skilled artisan could not have reasonably expected to obtain the claimed subject matter because the cited documents provide no guidance for obtaining an isolated human ANT3 polypeptide cultured from a host cell that comprises a recombinant expression construct as recited in the instant claims.

Applicants therefore further submit that neither of the cited documents, alone or in combination, teaches or suggests that an ordinarily skilled person would achieve Applicants' invention with any reasonable expectation of success. Applicants respectfully disagree with the assertion by the PTO that the claimed invention was within the ordinary skill in the art to make and use the claimed recombinant human ANT polypeptide according to methods described in the

cited documents in combination with any other prior art at the time the present invention was made.

Applicants submit that a person having ordinary skill in the art could not, in view of the art, reasonably have expected to express successfully either a yeast ANT polypeptide or a human ANT polypeptide in bacteria at the time Applicants' invention was made. Heimpel et al. (*J. Biol. Chem.* 276:11499-506 (2001)), a document available to the public only subsequent to the filing date of the present application, conclude that "the *E. coli* system does not express yeast AAC2 and mammalian AAC, such as human AAC1, due to unfavorable codon usage." (*See* Heimpel et al., at page 11504, first column). Even substitution of the unfavorable codons in the yeast AAC2-encoding polynucleotide, however, failed to increase expression in *E. coli* of the yeast transporter. Heimpel et al. further state that "renaturation/reconstitution of the AAC from inclusion bodies posed a challenge." (*See* page 11504, second column). Heimpel et al. thus provide evidence of failure by the art to express ANT in *E. coli* well after the filing date of the instant application (*see* U.S. Application No. 09/185,904, *supra*, particularly Action therein dated February 20, 2004, at page 3).

Applicants' invention is also nonobvious in view of Hatanaka et al. (*Biol. Pharm. Bull.* 24:595-99 (2001)), another document that exemplifies the state of the art well after the filing date of the present application. Hatanaka et al. describe that human ANT (AAC1) specific RNA was *not* expressed in the yeast recombinant expression system disclosed therein, and that only when human ANT amino-terminal coding sequences were replaced with yeast amino-terminal coding sequences was the chimeric yeast-human ANT polypeptide expressed in yeast mitochondrial membranes (*see* Hatanka et al., page 596-597). By contrast, in the present application, Applicants teach in a working example that human ANT-encoding RNA, without modification to include nucleotide sequences encoding a polypeptide tag for ANT detection or isolation, and without any other modification, was expressed in a yeast recombinant expression system (*see* page 83, line 13 through page 86, line 3).

Applicants respectfully submit that Hatanaka et al. and Heimpel et al. demonstrate that ordinarily skilled artisans, years after the filing date of the present application, were unsuccessful in making an isolated recombinant ANT polypeptide. Therefore, an ordinarily

skilled artisan at the time the present invention was made would not have combined the teachings of Cozens et al. and Adrian et al. successfully to achieve Applicants' invention.

Applicants also submit, as discussed in previous submissions of record, that nonobviousness of the claimed invention is supported by secondary factors such as a long-felt need and the failure of others to achieve Applicants' invention (*see* Declaration under 37 C.F. R. § 1.132 of Dr. Christen Anderson, submitted November 3, 2003). The Declarant discussed in detail the state of the art at the time Applicants' invention was made. Briefly, for example, Fiermonte et al. (*Biochem. J.* 294:293-99 (1993)) taught that while the oxyglutarate mitochondrial membrane transport protein could be expressed in bacteria, expression of ANT was toxic to bacteria, resulting in only low level expression of a non-functional ANT polypeptide. Miroux *et al.* (*J. Mol. Biol.* 260:289-98 (1996)) also attempted to express various recombinant proteins, including mammalian ANT, in a bacterial expression system but encountered multiple difficulties, including toxicity to host bacteria cells, poor solubility of the recombinant product, and accumulation of recombinant ANT in inclusion bodies (*e.g.*, Miroux et al., at pages 290-291 and Table 1). The state of the art *after* the date on which Applicants' invention was made, as exemplified by Heimpel et al. discussed herein, also illustrates the failure of others to make a recombinant ANT polypeptide that localizes to the mitochondrial membrane and is capable of binding to an ANT ligand.

Accordingly, Applicants respectfully submit that the present invention is nonobvious, satisfying the requirements of 35 U.S.C. § 103(a), and request that this rejection be withdrawn.

Applicants respectfully submit that all claims in the Application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned representative at (206) 622-4900.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC

Mae Joanne Rosok

Mae Joanne Rosok
Registration No. 48,903

Enclosures:

Second Supplemental Information Disclosure Statement
Form PTO-1449
2 references

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

484613_2